Fast and ultra-fast SFC analysis using the Agilent 1260 Infinity Analytical SFC System with the Aurora SFC-Fusion A5

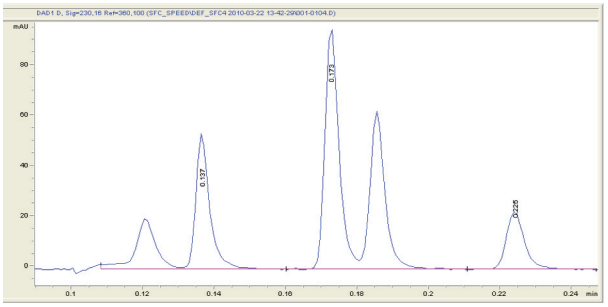
Effect of particle size and column length on speed

Application Note

Drug Development

Authors

Terry A. Berger and Blair K. Berger,
Aurora SFC Systems Inc,
Redwood City, CA
USA



Abstract

The Agilent Analytical Supercritical Fluid Chromatography system was used to demonstrate fast and ultrafast method development. High flow rates, sub-2-µm particle technology and short columns achieved separation times of less than 30 seconds with good resolution.

Introduction

Conventionally, analytical supercritical fluid chromatography (SFC) is performed on 5 µm particles with column dimensions in the order of 4.6 mm id and 25 cm in length. While these dimensions provide fast and efficient separations, higher throughput work is possible and desirable to increase sample throughput and to decrease cost of ownership. This Application Note explores the possibilities that modern column packing and dimensions offer for SFC applications.

Agilent Technologies

Experimental and results

The next generation of analytical SFC instruments, the Agilent 1260 Infinity Analytical SFC system containing the Aurora A5 Fusion and the Agilent 1260 Infinity Binary LC system delivers highly precise, stable chromatography. This is possible because of their tight mobile phase flow rate control with effective CO_2 precompression and back pressure regulation.

The Agilent 1260 Infinity Analytical SFC System (G4309A) contains the following components:

- Aurora Fusion A5
- Agilent 1260 Infinity SFC Binary Pump
- Agilent 1260 Infinity SFC High Performance Autosampler
- Agilent 1290 Infinity Thermostatted Column Compartment
- Agilent 1260 Infinity Diode Array Detector VL (80Hz < 0.01 min filter) with high pressure flow cell
- Agilent 1260 Infinity Vacuum Degasser

Higher separation speeds are achieved when column length is reduced, and flow rates are increased. Small particle size column packings can then be used to maintain the same resolution obtained with standard column packings. This is demonstrated in Figure 1. Peaks 3-4 have maintained a resolution value of approximately 1.3, from the first to last chromatogram. High separation efficiency between 100000 and 200000 plates per meter were obtained throughout the analysis.

In addition, the Agilent ZORBAX RX-Sil 4.6 mm × 50 mm column with 1.8 µm particles achieved ultrafast analysis with a gradient time of less than 30 s. A test mix of small drug-like molecules demonstrated ultra high speed and intermediate efficiency with symmetrical peaks. The last three peaks exhibited over 9000 plates each, and 650-1000 plates/sec. (Figure 2)

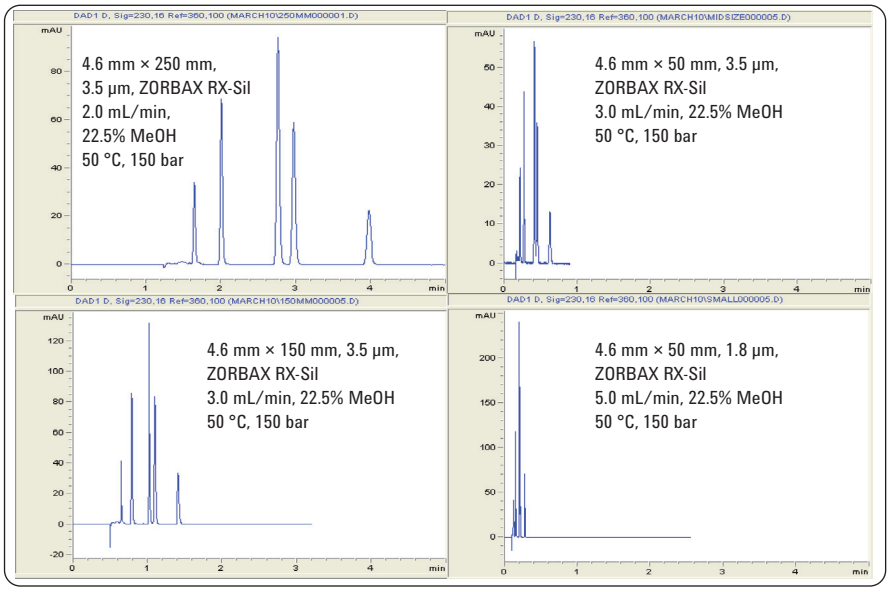


Figure 1
Method development for the separation of a 5 compound mixture using high flow rates and small column particles.

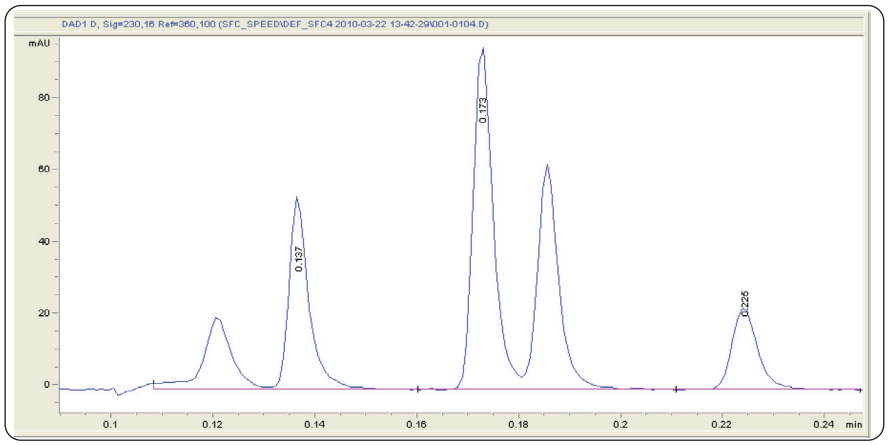


Figure 2
Ultra fast analysis of a five compound test-mixtures. Total gradient time is 14 seconds.

Conclusions

The Agilent Analytical SFC system separated a five-compound mixture in less than 30 s, as a result of its superior SFC technology and the beneficial physico-chemical properties of the supercritical fluidic mobile phase.

Dr. Terry Berger, founder of Aurora SFC Systems, has been a pioneer of Supercritical Fluid Chromatography for more than twenty-five years. His work has resulted in more than thirty patents and a host of journal publications. Since the mid-eighties he has systematically established fundamental research that expanded the theory and applicability of SFC.

www.agilent.com/chem/1200sfc

© Agilent Technologies, Inc., 2011
July 12, 2011
Publication Number 5990-6412EN

Agilent Technologies